PATENT COOPERATION TREATY

25. Okt. 2004

5781

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	22.10.2004
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
21418	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/10494 ✓	22.09.2003 ✓	27.09.2002

Applicant
DSM IP ASSETS B:V: et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 21418	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10494	International filing date *(day/month/year)* 22.09.2003	Priority date *(day/month/year)* 27.09.2002
International Patent Classification (IPC) or both national classification and IPC C12P17/04		
Applicant DSM IP ASSETS B:V: et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.03.2004	22.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Scott, J Telephone No. +31 70 340-2206

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10494

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-7 as originally filed

Claims, Numbers

1-6 received on 21.09.2004 with letter of 21.09.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1). Present Application

The present application relates to a process for the production of vitamin C from any of D-sorbitol, L-sorbose, L-sorbosone or L-gulose by (a) cultivating in an aqueous medium with Gluconobacter oxydans DSM 4025 (BP3812) then (b) isolating and purifying the vitamin C, *which is microbially produced directly from the fermentation broth.* This preferably takes place in a pH range of 4.0-9.0 and in a T range of 13-36°C for a time of 1 to 5 days.

2). Prior Art

Reference is made to the following documents:

D1 : EP - A - 0 832 974
D2 : US - A - 5 437 989

D1 discloses the production of 2-keto-L-gulonic acid from L-sorbose or D-sorbitol (p.3, l. 43-5) using G.oxydans strain DSM No. 4025. Moreover, L-sorbosone and D-gulose are also listed as converted (p.7, l.36 and 37). Vitamin C is easily produced from 2-keto-L-gulonic acid by methods known in the art (p.3, l.46-9).

D2 teaches the homogeneous alcohol/aldehyde dehydrogenase isolated from Gluconobacter oxydans strain DSM No. 4025 (FERM. BP-3812) is capable of catalysing the conversion of L-sorbose to 2-keto-L-gulonic acid via L-sorbosone at a pH between 7.0 and 9.0; at a T of 20-40°C (claim 1).

3). Novelty

The subject-matter of claims 1-6 of the present application is novel, in the sense of Article 33(2), PCT, over D1 and D2, by virtue of the fact that the vitamin C is microbially produced directly from the fermentation broth.

4). Inventive Step

The present application is novel by virtue of the fact that the vitamin C is microbially produced directly from the fermentation broth. The benefit of this is that the number of complex chemical steps is reduced, and the problem to be solved is the provision of an improved, simplified process for the production of vitamin C from a microorganism. The prior art documents do not detail the possibility of isolating vitamin C from the fermentation broth - indeed they do not even try - preferring to go via another chemical intermediate. In essence, they teach away from the solution the applicant has found - namely the direct isolation of vitamin C from the fermentation broth. Thus the subject matter of claims 1-6 is regarded as involving an inventive step in the sense of Article 33(3), PCT.

10/528893
JC14 Rec'd PCT/PTO 23 MAR 2005

1. A process for the production of vitamin C from D-sorbitol, L-sorbose, L-sorbosone or L-gulose comprising the steps of:

(a) cultivating a microorganism in an aqueous nutrient medium containing D-sorbitol, L-sorbose, L-sorbosone or L-gulose, wherein the microorganism is selected from the group consisting of *Gluconobacter oxydans* DSM 4025 (FERM BP-3812), a microorganism belonging to the genus *Gluconobacter* and having identifying characteristics of *G. oxydans* DSM 4025 (FERM BP-3812) and mutants thereof, and

(b) isolating and purifying the microbial produced vitamin C directly from the fermentation medium.

2. A process for the production of vitamin C from D-sorbitol, L-sorbose, L-sorbosone or L-gulose wherein a microorganism is cultivated in an aqueous nutrient medium containing D-sorbitol, L-sorbose, L-sorbosone or L-gulose and the microbially produced vitamin C is isolated directly from the fermentation broth and purified by conventional methods, said microorganism being selected from the group consisting of *Gluconobacter oxydans* DSM 4025 (FERM BP-3812), a microorganism belonging to the genus *Gluconobacter* and having identifying characteristics of *G. oxydans* DSM 4025 (FERM BP-3812) and mutants thereof.

3. A process according to claim 1 or 2 wherein the microorganism is *Gluconobacter oxydans* DSM 4025 (FERM BP-3812).

4. The process according to any one of the preceding claims wherein vitamin C is produced from L-gulose.

5. The process according to any one of the preceding claims, wherein the process is carried out at a pH in the range of about 4.0 to about 9.0 and in a temperature range from about 13°C to about 36°C for 1 to 5 days.

6. The process according to any one of the preceding claims, wherein the process is carried out at a pH in the range of about 5.0 to about 8.0 and at a temperature range from about 18° to about 33°C for 1 to 3 days.